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Randomized control trial of using tongue acupuncture in autism spectrum disorder

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Abstract *Objective:* The therapeutic approach of traditional chinese Medicine (TCM) in autism spectrum disorder (ASD) is a functional one. To study the efficacy, safety and functional brain change from the use of tongue acupuncture (TAC) on ASD children.
Methods: 21 autistic boys (3–16 years old) were randomly assigned to TAC group (TAC: $n = 12$; receiving daily TAC for 8 weeks) or control (C: $n = 9$; no acupuncture). Primary outcome measures included Autism Treatment Evaluation Checklist (ATEC), Reynell Language Developmental Scale, Symbolic Play Test (SPT), Functional Independence Measure for Children (WeeFIM), Clinical Global Impression (CGI) Scale and Cerebral FDG Metabolism by PET.
Results: There were significant improvement in speech domain of ATEC ($p = 0.030$), Self-care domain of WeeFIM ($p = 0.021$), cognition domain of WeeFIM ($p = 0.001$) and Total score domain of WeeFIM ($p = 0.001$) in TAC group compared to the C group. There were significant difference in positive clinical response between C and TAC group in language ($p = 0.0211$), functional ($p = 0.0011$), parental Impression criteria ($p = 0.0003$) and overall cerebral glucose metabolism ($p = 0.0451$) using ROC criteria. No significant association of PET Glucose Metabolism with Clinical response was found. None of the children developed any side-effects.

This randomized controlled trial was subsequently registered with the Clinical Trials.gov as the study had been completed in 2001(July 20, 2006; identifier: NCT00355329).
Autism Spectrum Disorder (ASD) and Autism will be used interchangeably in this paper.

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Conclusion: A short course of TAC can improve specific functions in children with autism spectrum disorder, especially speech and cognition function. No statistical significant association of PET Glucose Metabolism with Clinical response. Larger scale with more sample size trial should be done for further investigation.

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder affecting language, communication, social interaction, and behavior.[1] Autism is a heterogeneous disorder, commonly used therapies are a combination of specialized and supportive educational programming, communication training, psychosocial and behavioral and developmental interventions,[2–8] however no consensus can yet be made for the best treatment as there is great variability in the strength of evidence, ranging from an absence of evidence to anecdotal and no validation to varying extent.

In traditional Chinese acupuncture, nearly 400 acupoints on the body surface are interrelated to various functions. Acupuncture has been practiced in China for over 2 millennia. Specific acupoints in the tongue corresponding to various organs, and meridians were used for autism. The organ and meridian concept in the TCM model has been assumed as a fundamental basis to improve the behavior, cognition, and communicative ability in children with autism.

We have demonstrated clinical efficacy of acupuncturing the surface or base of the tongue in specific acupoints in improving various functional modalities in patients with chronic neurological disorders such as ASD, cerebral palsy, stroke, and drooling problems.[9–15] In our experience, the TCM approach for autism is more holistic. Autism is postulated as part of the spectrum of lower intelligence. Thus, the approach to autism is considered as lower intelligence due to "Heart-meridian and Kidney-meridian *yin-yang* imbalance" resulting in a communication problem and "Liver-meridian *yin-yang* imbalance" leading to behavioral problems.

Objective

We attempted to use a different approach in looking at autism and to assess the efficacy of an innovative method in TCM for improving the functional status of these children. The objective was to study the efficacy of a short course of tongue acupuncture (TAC) in improving the overall functional status of autism. This randomized controlled trial has been subsequently registered with the Clinical Trials.gov (July 20, 2006; identifier: NCT00355329) after completion of the study in 2001.

Ethical approval

This study was approved by the Ethics Committee of the Faculty of Medicine of the University of Hong Kong-Hong Kong West Cluster. The parents were informed about the methodology, and written consent was obtained.

Methods

Subjects

A total of 27 autistic boys were consecutively recruited from the Autism Research Clinic (Duchess of Kent Children Assessment Centre of Duchess of Kent Children Hospital) during 1998—2001.The inclusion criteria included a previous diagnosis of autism using standard criteria of the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) by our first author (V.W). Children with associated neurological disorders such as tuberous sclerosis, fragile X syndrome, and epilepsy were excluded. The age ranged between 3 and 16 years old.

All children were diagnosed as autism and had a comprehensive neurological and developmental evaluation by the first author (V.W.). All children were observed in an assessment setting, and a semi-structured diagnostic interview with the parents was made. Children were recruited only if they satisfied both criteria using the Autism Diagnostic Interview-Revised and with a score greater than 30 in the Childhood Autism Rating Scale (CARS).

Randomization and concealment allocation

27 Participants were randomized into two groups: Control group versus Tongue Acupuncture Treatment (TAC) group. Randomization was achieved by computer generation of C or TAC groups performed by independent statistician. They were randomly assigned to receive TAC. The conventional educational and behavioral model for autistic children was continued for both groups. Clinical assessor (V.W.) and Positron Emission Tomography (PET) scan assessor (D.W.C.Y.) were blinded to the randomization and allocation of groupings. Only the acupuncturist (J.G.S.) who performed TAC was not blinded.

Intervention

27 children attended our Tongue Acupuncture Research Clinic on an ambulatory basis. A total of 40 sessions (daily sessions) for a total course of 8 weeks were administered to TAC group. They were discharged immediately after the acupuncture session. All 27 children continued their conventional autism program.

In the TAC group, the patients received a total course of 40 sessions, with 5 daily sessions per week over 8 weeks,

while the patients in the C group did not have to visit the clinics 40 times because they just need to continue their scheduled training and education sessions.

TAC group (C) was applied to five specific acupoints on the tongue daily using a sterile disposable 0.3 × 4 cm acupuncture needle (Made in Guangzhou, China, Manufacturer, Hwato). Two acupoints at the center of the tongue surface (TAC #1 = *Run Ze*, 1 cm from the tongue tip and TAC #2 = *Guan Zhu*, 0.5 cm from the tongue tip) and three acupoints at the bottom of the tongue (i.e. sublingual region) (TAC #3 = *Tian Men*, center of the tongue base and TAC#4 and TAC #5 = *Di You'*, 0.5 cm from the tongue base on both sides) were punctured. The tongue surface TAC#1 was punctured by a 1 cm depth obliquely and TAC#2 about 0.3 cm depth obliquely. The bottom of the tongue TAC #3 was punctured perpendicularly by 0.5—1 cm depth and TAC #4 and #5 by 0.5 cm depth perpendicularly (Figs. 1—2).

The entire acupuncture procedure lasted for less than 15 seconds for each session. No sedation is required. No other stimulation was used. The child just sat on the mother's lap with the head tilted around 45° upwards. Sterile gauze was used to pick up and station the tongue with the examiner's left hand. The child was encouraged to open up his mouth. Quick and accurate insertion into five acupoints was performed with the examiner's right hand. Most children tolerated the procedure well. The children attended our TAC Research Clinic on an ambulatory basis. They were discharged immediately after TAC.

Blinded assessor assessment

The Following outcome measures were performed at baseline (week 0) and post-treatment (Week 8) in both groups by Clinical assessor (V.W.) and PET scan assessor (D.W.C.Y.)

1. Autism Treatment Evaluation Checklist (ATEC) consisting of four subscales (Speech, Sociability, Sensory/Cognitive Awareness, and Health/Physical/Behavior).

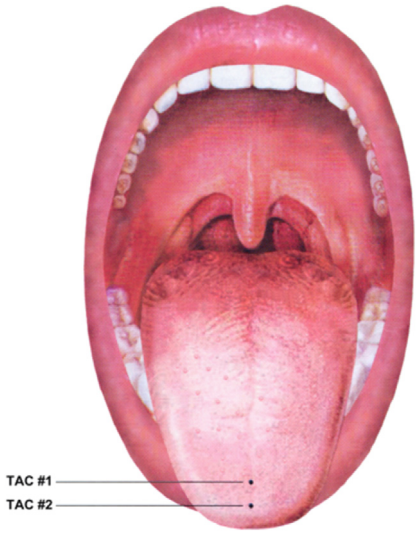

Figure 1 The location of the tongue acupuncture points (surface).

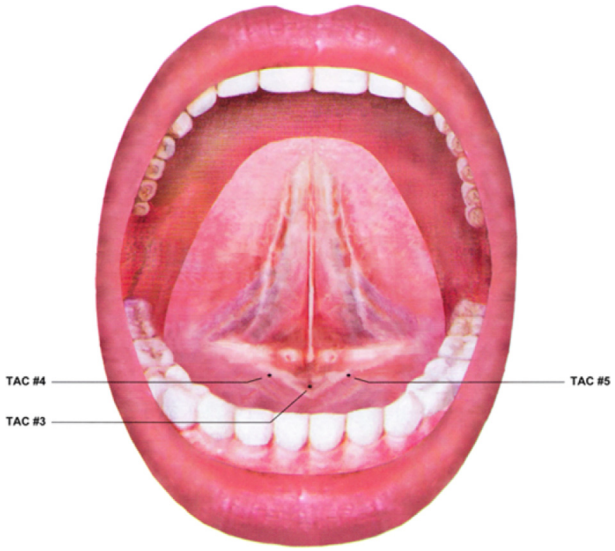

Figure 2 The location of the tongue acupuncture points (base).

2. Reynell Language Developmental Scale—Comprehension and Expression score, Comprehension and Expression age.
3. Symbolic Play Test (SPT)—total score and language age.
4. The WeeFIM® instrument—a functional independence measure for children with three domains of mobility, self-care and cognition.
5. Clinical Global Impression Scale (CGIS).
6. Cerebral FDG Metabolism by PET—18F-fluoro-deoxy-glucose (FDG) per 1.73 m2 body surface area with dose correction for blood glucose normalized to 5 mmol/L was injected. Such an approach tends to minimize variability caused by glucose level and body size.[16] If necessary, sedation with Lytic Cocktail will be given 25 min later, approximately 20 min prior to the PET scan. 3D brain PET scan is obtained using Siemen's ECAT Exact Scanner (Malvern, Philadelphia, 19355, USA) acquiring 120 million counts for emission and 50 million/5 min counts for transmission. PET scan was reconstructed using Order Subsets Estimation for Maximum Likelihood in 1 iteration and 30 subsets. Zoom factor was 2.5. Quality control was obtained for reproducibility of baseline and second scan in terms of blood glucose, mCi dose of FDG injected, time of performing FDG PET scan, time of sedation to minimize variation in the same patient and in between the C and T groups. There was no significant difference in these parameters between the T and C groups.

Twenty-two (22) regions of interest (ROIs) for each side of the brain were drawn on the FDG-PET scan with the assistance of a template by expert interaction, on the transverse slice images of the brain at different levels. The ROI includes right and left side of the superior/middle/inferior frontal gyri, precentral/postcentral gyri, superior/inferior parietal lobules, anterior/posterior cingulate gyri, Broca area, angular gyri, auditory temporal cortex, associative auditory temporal cortex, precuneus, cuneus, lingual gyri, hippocampus, cerebellum, pons, caudate head, lenfitorm nucleus, and thalamus.

Standardized Uptake Value maximum (SUVmax) and Standardized Uptake Value average (SUVavg) of each region were obtained. Cortical Mean SUVmax (CMSUVmax) and Cortical Mean SUVavg (CMSUVavg) were obtained for cortical lesions excluding the basal ganglia, thalamus, and cerebellar counts. An increase of 10% between baseline and post-treatment regional and CMSUVmax and CMSUVavg was considered a significant response.

Side-effects

The children were to be monitored for side-effects and the parents were asked to report on any change. A questionnaire on any side-effect was administered after the course of TAC treatment.

Statistical analysis

All data were collected before the codes of the treatment or control group were broken. The Receiver Operating Characteristic (ROC) curve was calculated to define a positive response for each assessment tool. After the ROC analysis, we found that ROC cut off for ATEC was >2, for Comprehension by Reynell, SPT and WeeFIM® responses are <2 and for CGIS was $<10\%$. After using the ROC criteria to calculate the number of children with positive response in each group, the difference in C and TAC groups was compared using the Fisher exact test. Comparison of difference between outcome measures of C and TAC groups with Fisher's exact test using ROC criteria. *P*-values for all statistical tests using unpaired Student's *t* test, Fisher's exact test were two-tailed and the results were considered as significant if $p < 0.05$.

Results

Baseline characteristics

The children were matched by mental or developmental age using Griffiths Mental Developmental Scale, language profile using Reynell Language Developmental Scale and/or Symbolic Play Test depending on the cognitive profile, social class status, and functional status using WeeFIM® score. There was no statistically significant difference between the two groups (Table 1).

Clinical outcome

Of 27 children recruited, only 21 were analyzed. Due to erroneous equipment calibration of the PET scanner by an engineer after an equipment maintenance service, 3 children from the TAC group and 1 child from the C group were excluded because of technical reasons. 1 child each from the TAC and C groups did not attend the second clinical assessment and repeated PET scanning. Thus, the final analysis consisted of 21 children with 12 and 9 from the TAC and C groups, respectively (Fig 3). The comparison of clinical outcome using standardized outcome measures is illustrated in Tables 2 and 3.

There were significant improvement in speech domain of ATEC ($p = 0.030$), Self-care domain of WeeFIM ($p = 0.021$),

Table 1 Baseline comparison of children with autism spectrum disorder.

	Control group ($n = 9$)			Treatment group ($n = 12$)			Unpaired student' *t* test
	Mean	Median	SD	Mean	Median	SD	*p* value
Age (y)	8.750	7.580	4.617	10.167	9.875	3.930	0.457
Autism Treatment Evaluation Checklist							
Speech/language/communication	14.111	12.000	7.524	11.500	11.500	6.654	0.41
Sociability	17.000	17.000	9.381	18.250	19.000	6.757	0.726
Sensory/cognitive awareness	18.556	18.000	6.064	16.917	16.500	5.418	0.522
Health/physical/behavior	14.000	12.000	8.201	14.000	13.000	7.261	1
Total	63.667	62.000	24.403	59.833	58.500	19.197	0.691
Griffiths Mental Developmental Scale							
Mental age (m)	51.133	53.700	17.744	69.375	74.850	24.780	0.077
General quotient	60.361	60.600	29.914	60.379	56.950	17.958	0.999
Reynell Language Developmental Scale							
Comprehension score	30.000	29.000	18.648	43.917	49.000	22.781	0.152
Comprehension age (y)	2.889	2.580	1.723	4.318	4.103	2.265	0.131
Expression score	25.111	15.000	20.393	38.750	42.500	19.661	0.138
Expression age (y)	2.395	1.670	1.875	3.388	3.165	1.770	0.23
Symbolic Play Test							
Total score	11.444	10.000	9.275	16.000	18.500	7.734	0.235
Language age (m)	22.133	19.300	10.620	27.458	30.450	9.243	0.235
WeeFIM (Functional Quotient)							
Self Care	82.811	78.700	10.067	88.208	91.950	12.377	0.299
Mobility	94.333	99.500	11.219	95.750	100.000	6.874	0.738
Cognition	41.644	34.300	17.141	47.983	42.500	15.561	0.387
Total	74.811	71.400	10.168	79.133	79.400	9.002	0.316

y, years; m, months; WeeFIM, Functional Independence Measure for children.

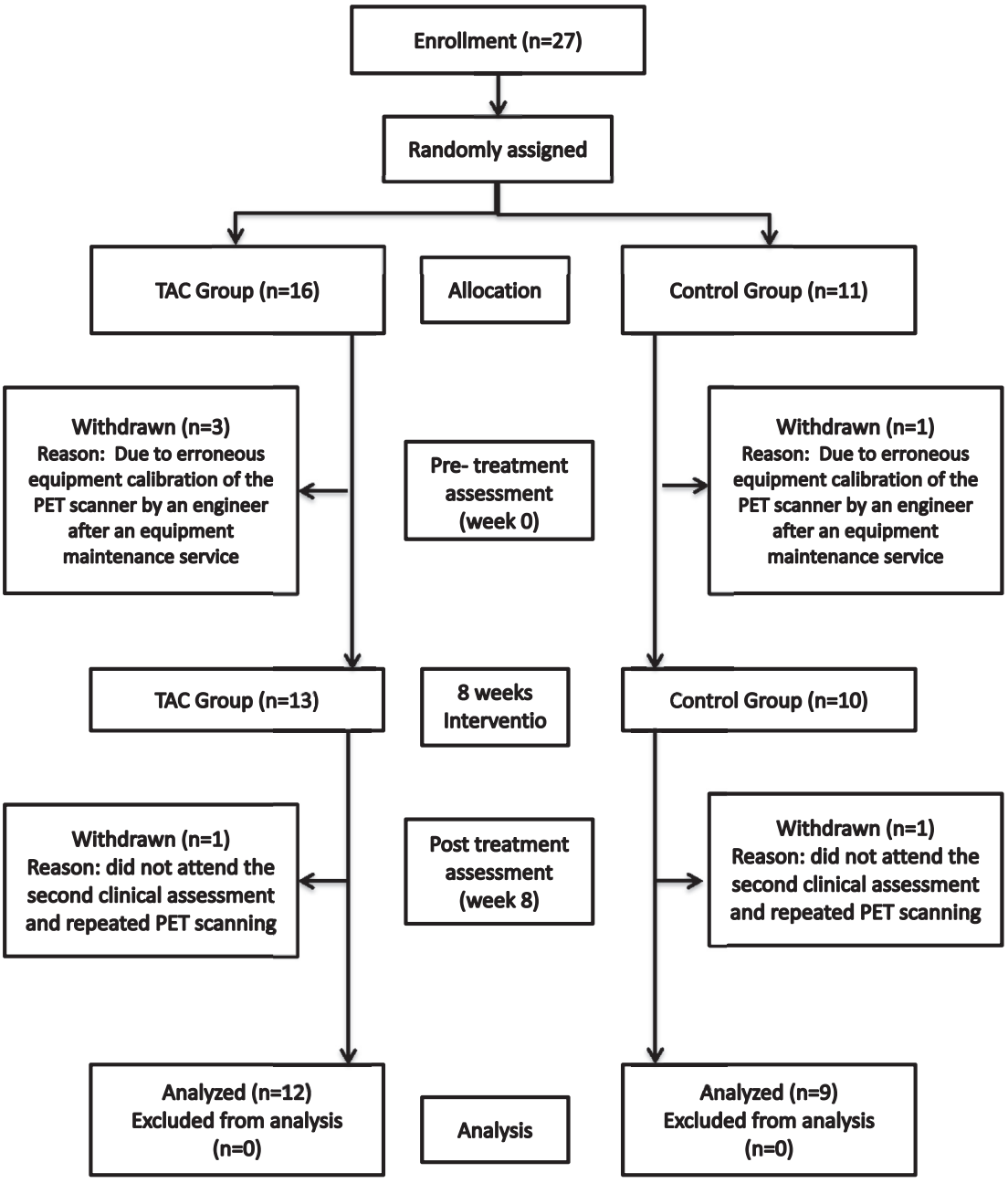

Figure 3 Flow chat of the study.

cognition domain of WeeFIM ($p = 0.001$) and Total score domain of WeeFIM ($p = 0.001$) in the TAC group compared to the C group. There was significant difference in positive clinical response between the C and TAC group in language ($p = 0.0211$), functional ($p = 0.0011$), parental Impression criteria ($p = 0.0003$) and overall cerebral glucose metabolism ($p = 0.0451$).

PET glucose metabolism

Using a criterion of $\geq$10% increase in CMSUVmax and CMSUVavg as a significant change in PET glucose metabolism between the baseline and post-intervention PET scan, 5/12 (42%) in the TAC group had an increase in both SUVmax and SUVavg, while none in the C group shows such change. Fisher's exact test statistical analysis indicated that the difference has significant ($p = 0.0451$).

The PET scans of the 5 positive cases in the TAC group are illustrated in WeeFIM®. There are no association between PET glucose metabolism and clinical response (Table 4).

As far as regional metabolic change, significant increase in percentage of SUVmax between the second PET and the baseline PET is noted in the following regions: left superior frontal gyrus ($p = 0.0184$), left precentral gyrus ($p = 0.278$), left post-central gyrus ($p = 0.0409$), left posterior cingular gyrus ($p = 0.0491$), right precuneus ($p = 0.0227$), left angular gyrus ($p = 0.0227$), right caudate head ($p = 0.0491$), right thalamus ($p = 0.0491$), right post GTS (Table 5).

Table 2 Comparison of therapeutic effect of control and treatment groups using unpaired *t* test.

	Control group ($n = 9$) (post-pre)			Treatment group ($n = 12$) (post-pre)			Unpaired student' *t* test
	Mean	Median	SD	Mean	Median	SD	*p*-value
Autism Treatment Evaluation Checklist							
Speech/language/communication	−0.333	−1.000	2.121	−3.167	−2.500	3.099	0.030*
Sociability	−1.000	−1.000	3.464	−3.500	−2.500	6.708	0.322
Sensory/cognitive awareness	0.222	0.000	3.768	−2.250	−1.500	4.070	0.172
Health/physical/behavior	−1.556	−1.000	2.833	−1.750	−1.000	3.745	0.898
Total	−2.667	−2.000	7.665	−9.833	−9.000	13.570	0.172
Reynell Language Developmental Scale							
Comprehension score	2.889	3.000	2.804	5.333	3.500	6.169	0.285
Comprehension age (y)	0.177	0.170	0.225	0.678	0.210	1.041	0.174
Expression score	3.222	0.000	4.790	5.250	5.500	3.957	0.301
Expression age (y)	0.230	0.000	0.465	0.795	0.415	0.879	0.097
Symbolic Play Test							
Total score	0.889	1.000	1.054	2.250	2.000	3.251	0.244
Language age (m)	0.656	0.000	1.300	2.533	1.350	4.304	0.223
WeeFIM (Functional Quotient)							
Self Care	−2.222	0.000	4.645	1.875	0.000	2.815	0.021*
Mobility	0.056	0.000	0.167	1.833	0.000	5.437	0.342
Cognition	1.956	0.500	2.316	9.867	11.450	5.637	0.001*
Total	−0.078	0.000	1.434	3.875	3.200	2.892	0.001*

* Significant difference between control group and treatment group.
y, years; m, months; WeeFIM, Functional Independence Measure for children.

Side-effect

None of the children developed any side-effects. Initial crying for fear and possible minor pain occurred in the first few sessions in some children. However, most children adapted easily and tolerated the technique well.

Discussion

We have demonstrated a randomized control trial with innovative traditional Chinese medicine method (short consecutive course of TAC over 8 weeks) can improve the functional status of children with autism. There is significant

Table 3 Comparison of difference in positive clinical response between control and treatment groups using fisher's exact test.

Outcome measure used	Control ($n = 9$)		Treatment ($n = 12$)		*p* value	Odd ratio (OR)	95% or
	Positive response with ROC criteria	No response with ROC criteria	Positive response with ROC criteria	No response with ROC criteria	(Fisher's exact test)		
Behavioral Autism Treatment Evaluation Checklist (ATEC)	5	4	11	1	0.1194	8.8	0.772—100.32
Language Comprehension using Reynell Comprehension using SPT	5	4	12	0	0.0211*	20.455	0.9309—449.46
Functional WeeFIM (Functional Quotient)	0	9	9	3	0.0011*	51.571	2.329—1141.8
Parental Impression Criteria Clinical Global Impression Scale (CGIS)	2	7	12	0	0.0003*	75	3.153—1784.2
Overall cerebral glucose metabolism PET scan of brain	0	9	5	7	0.0451*	13.933	0.6599—294.21

*Significant difference between control and treatment groups.
Noted that at least one value is zero. To make calculations possible, 0.5 was added to each value.
Receiver Operating Characteristic (ROC) curve; SPT, Symbolic Play Test; WeeFIM, Functional Independence Measure for children; PET, positron emission tomography.

Table 4 Association of PET glucose metabolism with clinical response using fisher's exact test.

	PET positive ($n = 5$)	PET negative ($n = 16$)	*P*-value (Fisher's exact test)	Or	95% or
Behavioral					
ATEC Positive	4 (80%)	12 (75%)	1	1.333	0.133–15.704
ATEC Negative	1 (20%)	4 (25%)			
Language Expression					
Reynell (Expression) Positive	4 (80%)	9 (56%)	0.606	3.111	0.281–34.419
Reynell (Expression)Negative	1 (20%)	7 (44%)			
Language comprehension					
Reynell and SPT Positive	2 (40%)	5 (31%)	1	1.467	0.184–11.718
Reynell and SPT Negative	3 (60%)	11 (69%)			
Functional					
WeeFIM Positive	3 (60%)	6 (38%)	0.611	2.5	0.32–19.529
WeeFIM Negative	2 (40%)	10 (63%)			

improvement in the functional domains such as speech, self-care and cognition, which has matched the similar findings in recent research in this field. There is improved glucose uptake in 42% (5 of 12) of TAC group subject compared to 0% (0 of 9) in control group. As this is a pilot study, a small sample size may be the reason why there is no significant association of PET Glucose metabolism with clinical response when used as a surrogate marker for brain function.

Using PET study with FDG as a treatment outcome in children with autism spectrum disorder is rare.[6,11,17–22] The results were still conflicting, partly due to the different diagnostic criteria, wide age range, sex difference, and variability in cognitive or language abilities. Quantitative analysis of local glucose metabolism showed that the brain follows a protracted glucose metabolic maturational course.[23] Limited studies of neurotransmitter-PET in autism have shown asymmetry of cerebral hemispheres in serotonin metabolism of the frontal cortex, thalamus, and dentate nucleus of the cerebellum[17] and hypometabolism of serotonin might explain some symptoms of autism. F-Dopa uptake was also found to be reduced in the medial prefrontal cortex.[24] Some researchers explained the nature of the underlying brain dysfunction of childhood autism and reveal a localized dysfunction of the temporal lobes in children with idiopathic autism by using functional brain imaging.[25] The limbic, posterior associative and cerebellar cortices showed increased blood flow in ASD.[22]

Magnetic resonance imaging (MRI) studies have shown that the neocerebellar vermal lobules VI and VII were hypoplastic in both retarded and nonretarded autism.[18] The neocerebellum may affect the brainstem, hypothalamus, and thalamus via its connections, thus affecting cognitive, sensory, autonomic, and motor activities.[23,26–29] A whole brain analysis of MRI demonstrated decrease in gray matter of the anterior systems (right paracingulate sulcus and left inferior frontal gyrus) and increase in the posterior parts (amygdala/peri-amygdaloid cortex, middle temporal gyrus, and inferior temporal gyrus) and cerebellum. This study provides convergence evidence of the physiologic basis of social cognition because these structures are implicated in social cognition in both animal imaging and histopathologic studies.[30] High-resolution MRI study had shown increase volume of caudate nuclei in autism as compared to controls, and the caudate may be part of the abnormal neural network contributing to ritualistic–repetitive behavior.[31]

Functional MRI had demonstrated that there might be a network of neural regions that compose the "social brain", accounting for social intelligence independent of general intelligence, which consisted of the orbitofrontal cortex, superior temporal gyrus, and amygdala. Asperger syndrome showed lack of activation in the amygdala but some activation of frontotemporal regions. This explained the social brain theory of normal function and the amygdala theory of autism.[32]

We have demonstrated that the cortical mean glucose uptake shows statistically significant improvement in 42% patients of the T group as compared with none in the C group. The increase in glucose metabolism is more marked on the left side of the brain in frontal, cingulate gyrus, angular gyrus, auditory association cortex, precuneus, and both thalami (Fig. 4). We postulate that with TAC stimulation to the central neural network in both thalami, a further networking with visual, auditory, and attentional areas of the brain may explain the clinical improvement in communication, attention, and cognition. This surrogate increase in glucose metabolism shown in the PET scan did not show any correlation with clinical improvement in behavioral, language, and functional levels. The change in glucose metabolism in the PET scan provides an objective measurement which does not have any clinical correlation. Further detailed analysis of the metabolic change at different regions of the brain will require future work utilizing statistical parametric mapping software analysis. We thus postulate that autism is a clinical cognitive and behavioral phenotype due to dysfunction to various degrees in neural networking connecting one or both frontal, temporal lobes with/without connecting network to parietal, occipital lobes, cerebellum, and basal ganglia via the central relay station in the thalamus. Thus, repetitive neural stimulation with acupuncture, especially in the tongue with the shortest neural pathway to the cerebellum currently postulated as our "social brain", revitalizes the neural plasticity to other dysfunctional regions via the thalamus. We postulate that specific tongue acupoints may be related to various functional domains of the human body, similar to "the human topography in the motor and sensory cortex of the frontal and parietal lobes".

Table 5 Comparison of brain PET scan SUVmax in different region between control and treatment groups using Mann-Whitney test.

Brain region name	Control group ($n = 9$) (post-pre)			Treatment group ($n = 12$) (post-pre)			Mann—Whitney test
	Mean	Median	SD	Mean	Median	SD	*P*-value
Right Gyra frontal superioris (GFS)	−0.5	−0.7	7.6276	9.967	9.25	16.8821	0.1694
Left GFS	−3.611	−2.9	9.6001	13.417	11.55	19.355	0.0184*
Right Gyra frontal medius (GFM)	21.2217	−1.3	8.2487	10.325	6.2	−2.389	0.0955
Left GFM	0.256	0.3	9.1043	13.717	7.6	21.6459	0.1694
Right Precentral gyrus (PRE)	−2.656	−0.5	9.6613	6.533	6.6	16.825	0.1930
Left PRE	−3.256	−2.3	6.3683	10.025	5.35	18.796	0.0278*
Right Premotor (GFI)	−2.667	−1	8.449	7.983	9.25	16.4619	0.0693
Left GFI	0.067	−0.6	6.0129	8.708	3.85	19.094	0.2188
Right Post—central gyrus (PCG)	−2.111	−0.9	9.3292	6.592	4.65	19.4867	0.2469
Left PCG	−3.644	−4.4	10.0251	11.442	11.1	23.3105	0.0409*
Right Lobus parietal inferioris (LPI)	−4.133	−1.6	11.697	8.192	9.75	16.1577	0.0815
Left LPI	−4.456	−6.4	11.7105	7.717	7.45	20.6089	0.1479
Right Lobus parietal superioris (LPS)	−3.522	−3.1	10.8358	10.05	12.7	18.5712	0.1694
Left LPS	−1.533	−2.4	10.0502	8.825	9.45	20.8003	0.2773
Right Anterior cingulate gyrus (AGC)	−0.422	0.6	6.8117	9.208	3.1	18.9667	0.2188
Left AGC	1.7	4.6	11.3443	8.125	−1.7	23.6689	0.7021
Right Posterior cingulate gyrus (PGC)	−2.889	−1.4	9.0946	10.825	6.6	19.285	0.0815
Left PGC	−1.9	−2	12.8111	14.283	10.4	18.9587	0.0491*
Right Precuneus (PCUN)	−3.4	−1.7	6.9331	12.117	5.75	21.2696	0.0227*
Left PCUN	−5.967	−4.2	7.796	7.258	1.85	17.2241	0.0585
Right Angular gyrus	−1.333	1	9.0763	6.867	6.55	15.219	0.1694
Left Angular gyrus	−1.433	−1	8.0706	11.017	6.85	15.6506	0.0227*
Right Frontal operculum	−2.344	−0.6	8.2283	9.508	6.6	17.8294	0.0585
Left Frontal operculum (Brocca)	−2.9778	−0.7	10.36409	9.6333	2	21.28253	0.2188
Right Caudate head (CAU)	−5.4333	−4.9	10.45897	8.5667	3	20.76349	0.0491*
Left CAU	−0.8778	2.9	13.91652	6.225	2.15	14.11853	0.5079
Right Thalamus (THA)	−6.5222	−4.7	13.55644	12.6	5.75	19.51219	0.0491*
Left THA	−3.0556	−4	11.23656	12.45	5	20.58797	0.0815
Right Cuneus (CUN)	−1.3556	−3.1	11.16357	6.0417	2.4	24.03227	0.5538
Left CUN	−0.6222	3	12.08737	7.4667	2.95	23.82651	0.7544
Right. Lentiform (LEN)	−2.7111	−0.3	10.12132	5.3	−0.8	19.72737	0.6016
Left LEN	−2.5222	−2	12.59948	9.625	4.9	23.74138	0.2773
Right Primary visual cortex (Lingual)	−1.3556	−0.2	7.85384	8.45	8.75	18.52298	0.2469
Left CAL	−0.8222	0.3	5.40249	7.4667	6.2	17.01023	0.2188
Right Primary auditory cortex	−1.2222	1.3	9.29392	8.4167	5.4	19.7612	0.2773
Left PAC(Wernicke area)	−3.5889	−6.6	9.78742	11.1417	7.6	20.3563	0.0585
Right. Auditory association cortex (GTS)	−1.5889	0.5	10.09944	10.7083	8.5	18.08804	0.1111
Left Posterior GTS	−4.2333	−3.9	9.97547	13.1583	13	19.07585	0.0118*
Right Mesiotemporal hippocampus (HIP)	−0.9111	0.1	6.4843	10.075	9.45	17.94087	0.0815
Left HIP	−4.6111	−6.5	11.03024	7.2833	5.65	19.28267	0.1694
Right Cerebellum (CBLL)	−3.1444	−4.3	10.28386	7.6833	−0.05	20.42542	0.1930
Left CBLL	−3.2444	−2.8	6.55574	7.0833	1.9	10.86079	0.3100
Right Pons	−1.5111	0.1	10.20704	7.3917	−0.65	21.22059	0.6511
Left Pons	−1.4556	0.1	8.56141	9.7333	1.8	18.46881	0.1830

*Significant difference between control and treatment groups

Improvement in alertness, attention, and emotional state of a child through "starting-up" with TAC to acupoints rich in neural networking to the frontal cortex through the thalamus may explain the improvement in the child's awareness or attention. Thus, by a mechanism of re-networking of the "brain systems," plasticity of the brain can be regained.

In the TCM model, there are 14 meridians and 400 more acupoints (including 361 acupoints from 14 meridians and 48 extra acupoints) in the human body. The acupoints in the tongue correspond to various organs and meridians of the human body. This, in turn, is linked to various diseases, according to the *Zung-Fu* concept (or the "organ" concept). If we approach neurological diseases using a functional point of

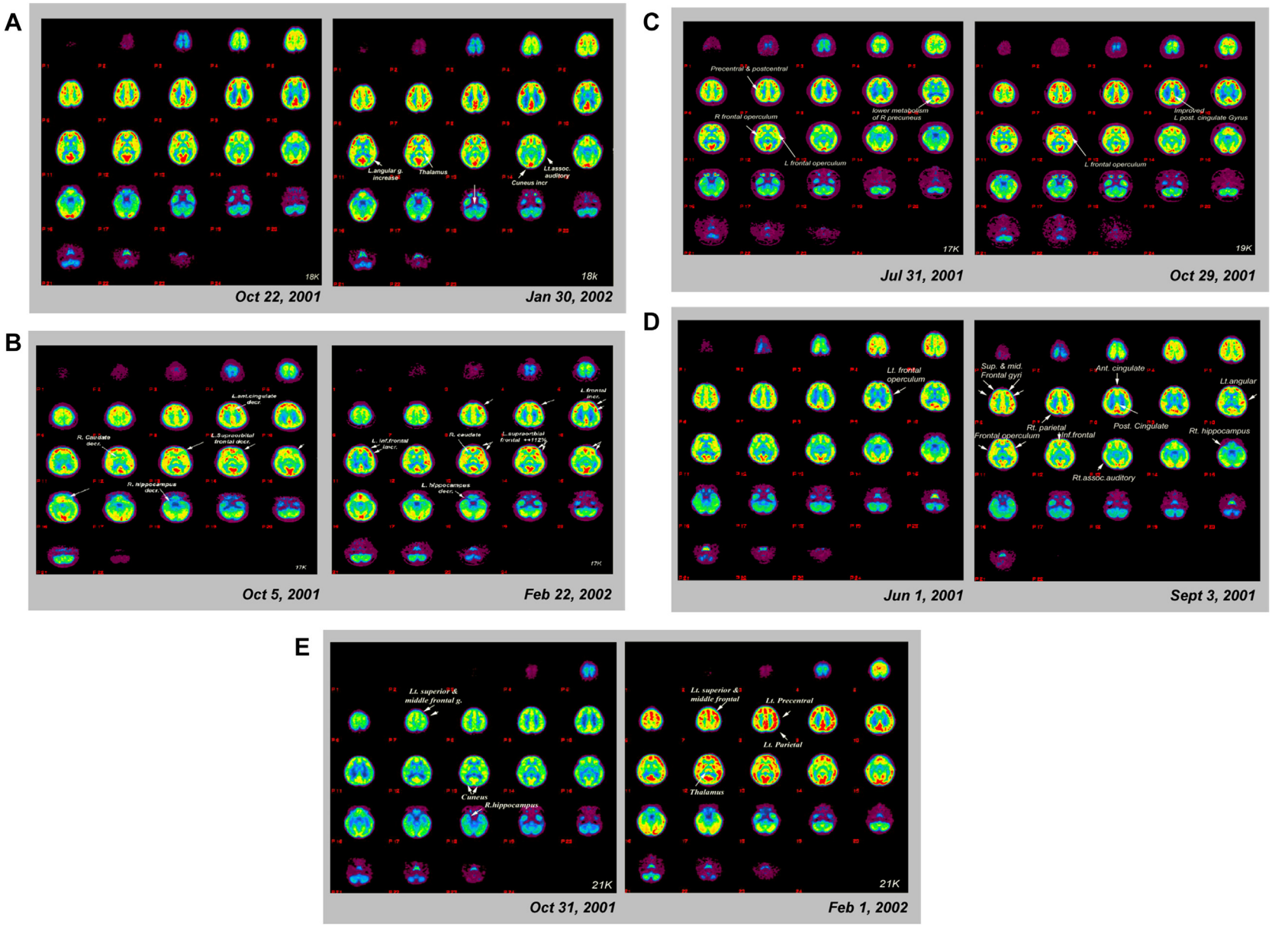

Figure 4 Five case studies with positive positron emission tomography (PET) response of brain pre- (left hand side) and post- (right-hand side) tongue acupuncture treatment **A**: Case 1 (Wong KC; M/8 y). **B**: Case 2 (Ho KK; M/14 y). **C**: Case 3 (Ng HL; M/15 y). **D**: Case 4 (Chau YH; M 6 y). **E**: Case 5 (Ip AJ; M 10 y).

view according to the TCM model, then stimulating the acupoints will improve functions in various aspects (e.g. communication skills, cognition, sleeping pattern, appetite, and behavior). This is a new way to look at autism from the TCM philosophy. Tongue is full of neural networks and the connection between the tongue and the brain (cerebellum, frontal, and temporal lobe may reinnervate other neural pathways gradually with repetitive stimulation). Thus, by innervating various key acupoints in the tongue, the overall general function of a child may be improved. The improvement of function may not be directly related to autism, but a general improvement of the overall functional ability of a person as the basis of improvement. The reinnervation of the neural network may help to reestablish the link with any dormant neural networks, thus compensating for the problems considered the core features autism.

In Western medicine with its long scientific background, the tongue occupies a relatively larger topography in the homunculus of the motor and sensory cortex than the rest of the body parts by proportion. The tongue is a very important organ in the body. It facilitates the function of biting, swallowing, sense of taste, production of speech, and emotion through local contact and neural connection with various lobes of the brain. The tongue is rich in neural (glossopharyngeal and vagus nerves), vascular, and lymphatic supply. Thus, by single or repetitive superficial or deep stimulation to the tongue using acupuncture needles to acupoints, the key and core centers for linking the vascular—lymphatic—neural networking might be ignited. The physiologic basis of efficacy of TAC in terms of immediate, intermediate, or long-term effects might be explained by resignaling and potentiation of neural receptors or neurotransmitters through repeated direct stimulation. Thus, the holistic approach has a neurophysiologic basis, possibly by igniting the key brain center (e.g. the thalamus), via the close neural network of the tongue to the cerebellum, and brainstem, with its vast networking to all regions of the brain.

Thus, while approaching autism from a Western medical model, one should also analyze the functional improvement in autism from a TCM perspective. Thus, we consider TAC a "start-up" program for children with autism. Of course, after "switching on" the brain with neural stimulation, it is necessary to intensify the effect with a continuous Western model of treatment of autism-like behavior modification or education modeling.

This is a pilot study, and it is quite impossible to launch multicenter trials with interventional skills such as acupuncture because the standardization of the technique requires experience and skills in handling autistic children. Thus, there may be subgroups of children with autism who respond better. Our 5 cases with positive PET glucose response belong to the milder subtypes. Thus, subgroups of autism should be studied to ascertain the efficacy of acupuncture in autism. We still need to assess other factors contributing to efficacy, in terms of any intermediate, sustained, or long-term efficacy.

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